

Attorney Docket No.: DOC-0216US (ISIS.003CPI)
US\$N 10/712,795

AMENDMENTS TO THE CLAIMS

LISTING OF THE CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application.

1-108 (Canceled)

109. (New) An antisense compound 12 to 30 nucleobases in length, wherein said compound specifically hybridizes with up to two mismatches to a sequence in the range of nucleotides 3230-3288 as set forth in SEQ ID NO:3.

110. (New) The antisense compound of claim 109, which is 14 to 20 nucleotides in length.

111. (New) The antisense compound of claim 109, which is an antisense oligonucleotide.

112. (New) The antisense oligonucleotide of claim 111, wherein the antisense oligonucleotide comprises at least one modified internucleoside linkage.

113. (New) The antisense oligonucleotide of claim 112, wherein the modified internucleoside linkage is a phosphorothioate linkage.

114. (New) The antisense oligonucleotide of claim 111, wherein the antisense oligonucleotide comprises at least one modified sugar moiety.

115. (New) The antisense oligonucleotide of claim 114, wherein the modified sugar moiety is a 2'-O-methoxyethyl sugar moiety.

116. (New) The antisense oligonucleotide of claim 114, wherein the modified sugar moiety is a bicyclic sugar moiety.

117. (New) The antisense oligonucleotide of claim 111, wherein the antisense oligonucleotide is a chimeric oligonucleotide having a plurality of 2'-deoxynucleotides flanked on each side by at least one nucleotide having a modified sugar moiety.

118. (New) The antisense oligonucleotide of claim 117, wherein the modified sugar moiety is a 2'-O-methoxyethyl sugar moiety.

119. (New) The antisense oligonucleotide of claim 117, wherein the modified sugar moiety is a bicyclic sugar moiety.

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120. (New) The antisense oligonucleotide of claim 111, wherein the antisense oligonucleotide comprises at least one modified nucleobase.
121. (New) The antisense oligonucleotide of claim 120, wherein the modified nucleobase is a 5-methylcytosine.
122. (New) The antisense compound of claim 109, wherein the antisense compound is in a salt form.
123. (New) The antisense compound of claim 122, wherein the antisense compound is a sodium salt.
124. (New) A composition comprising the antisense compound of any one of claims 109-123 and a pharmaceutically acceptable carrier or diluent.
125. (New) An antisense oligonucleotide 12 to 30 nucleobases in length comprising at least 8 contiguous nucleotides of SEQ ID NO:247.
126. (New) The antisense oligonucleotide of claim 125, fourteen to twenty nucleobases in length.
127. (New) The antisense oligonucleotide of claim 125, wherein the antisense oligonucleotide has a sequence comprising SEQ ID NO:247.
128. (New) The antisense oligonucleotide of claim 125, wherein the antisense oligonucleotide has a sequence consisting of SEQ ID NO:247.
129. (New) The antisense oligonucleotide of claim 125, wherein the antisense oligonucleotide comprises at least one modified internucleoside linkage.
130. (New) The antisense oligonucleotide of claim 129, wherein the modified internucleoside linkage is a phosphorothioate linkage.
131. (New) The antisense oligonucleotide of claim 125, wherein the antisense oligonucleotide comprises at least one modified sugar moiety.
132. (New) The antisense oligonucleotide of claim 131, wherein the modified sugar moiety is a 2'-O-methoxyethyl sugar moiety.

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133. (New) The antisense oligonucleotide of claim 131, wherein the modified sugar moiety is a bicyclic sugar moiety.
134. (New) The antisense oligonucleotide of claim 125, wherein the antisense oligonucleotide is a chimeric oligonucleotide having a plurality of 2'-deoxynucleotides flanked on each side by at least one nucleotide having a modified sugar moiety.
135. (New) The antisense oligonucleotide of claim 134, wherein the modified sugar moiety is a 2'-O-methoxyethyl sugar moiety.
136. (New) The antisense oligonucleotide of claim 134, wherein the modified sugar moiety is a bicyclic sugar moiety.
137. (New) The antisense oligonucleotide of claim 125, wherein the antisense oligonucleotide comprises at least one modified nucleobase.
138. (New) The antisense oligonucleotide of claim 137, wherein the modified nucleobase is a 5-methylcytosine.
139. (New) The antisense oligonucleotide of claim 125, wherein the antisense oligonucleotide is in a salt form.
140. (New) The antisense oligonucleotide of claim 139, wherein the antisense oligonucleotide is a sodium salt.
141. (New) A composition comprising the antisense oligonucleotide of any one of claims 125-140 and a pharmaceutically acceptable carrier or diluent.
142. (New) An antisense oligonucleotide 20 nucleobases in length having a sequence of nucleobases as set forth in SEQ ID NO:247 and comprising 5-methylcytidine at nucleobases 2, 3, 5, 9, 12, 15, 17, 19, and 20, wherein every internucleoside linkage is a phosphorothioate linkage, nucleobases 1-5 and 16-20 are 2'-O-methoxyethyl nucleotides, and nucleobases 6-15 are 2'-deoxynucleotides.
143. (New) The antisense oligonucleotide of claim 142, wherein the antisense oligonucleotide is in a salt form.
144. (New) The antisense oligonucleotide of claim 143, wherein the antisense oligonucleotide is a sodium salt.

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145. (New) A composition comprising the antisense oligonucleotide of any of claims 142 - 144 and a pharmaceutically acceptable carrier or diluent.
146. (New) A method of lowering serum cholesterol levels in a human comprising administering to said human a therapeutically effective amount of the antisense compound of claim 109.
147. (New) The method of claim 146, wherein the serum cholesterol levels are serum LDL-cholesterol levels.
148. (New) The method of claim 146, wherein the serum cholesterol levels are serum VLDL-cholesterol levels.
149. (New) The method of claim 146, wherein the serum cholesterol levels are serum total cholesterol levels.
150. (New) A method of lowering lipoprotein levels in a human comprising administering to said human a therapeutically effective amount of the antisense compound of claim 109.
151. (New) The method of claim 150, wherein the lipoprotein levels are low density lipoprotein levels.
152. (New) The method of claim 150, wherein the lipoprotein levels are very low density lipoprotein levels.
153. (New) The method of claim 150, wherein the lipoprotein levels are Lipoprotein(a) levels.
154. (New) A method of lowering serum apolipoprotein B levels in a human comprising administering to said human a therapeutically effective amount of the antisense compound of claim 109.
155. (New) The method of claim 154, wherein the serum apolipoprotein B is apolipoprotein B-100.
156. (New) A method of treating a human having a cardiovascular disease or disorder comprising administering to said human a therapeutically effective amount of the antisense compound of claim 109.

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157. (New) The method of claim 156, wherein the disease or disorder is abnormal lipid metabolism, abnormal cholesterol metabolism, or abnormal triglyceride metabolism.
158. (New) The method of claim 156, wherein the disease or disorder is hypercholesterolemia, hyperlipidemia, or hypertriglyceridemia.
159. (New) The method of claim 156, wherein the disease or disorder is atherosclerosis.
160. (New) The method of claim 156, further comprising a step of measuring serum LDL-cholesterol, serum VLDL-cholesterol, serum total cholesterol, serum apolipoprotein B, serum triglycerides, or serum Lipoprotein(a).
161. (New) The method of any one of claims 146-160, wherein the antisense compound is administered intravenously.
162. (New) The method of any one of claims 146-160, wherein the antisense compound is administered subcutaneously.
163. (New) A method of lowering serum cholesterol levels in a human comprising administering to said human a therapeutically effective amount of the antisense oligonucleotide of claim 125.
164. (New) The method of claim 163 wherein the serum cholesterol levels are serum LDL-cholesterol levels.
165. (New) The method of claim 163, wherein the serum cholesterol levels are serum VLDL-cholesterol levels.
166. (New) The method of claim 163, wherein the serum cholesterol levels are serum total cholesterol levels.
167. (New) A method of lowering lipoprotein levels in a human comprising administering to said human a therapeutically effective amount of the antisense oligonucleotide of claim 125.
168. (New) The method of claim 167, wherein the lipoprotein levels are low density lipoprotein levels.

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169. (New) The method of claim 167, wherein the lipoprotein levels are very low density lipoprotein levels.
170. (New) The method of claim 167, wherein the lipoprotein levels are Lipoprotein(a) levels.
171. (New) A method of lowering serum apolipoprotein B levels in a human comprising administering to said human a therapeutically effective amount of the antisense oligonucleotide of claim 125.
172. (New) The method of claim 171, wherein the serum apolipoprotein B is apolipoprotein B-100.
173. (New) A method of treating a human having a cardiovascular disease or disorder comprising administering to said human a therapeutically effective amount of the antisense oligonucleotide of claim 125.
174. (New) The method of claim 173, wherein the disease or disorder is abnormal lipid metabolism, abnormal cholesterol metabolism, or abnormal triglyceride metabolism.
175. (New) The method of claim 173, wherein the disease or disorder is hypercholesterolemia, hyperlipidemia, or hypertriglyceridemia.
176. (New) The method of claim 173, wherein the disease or disorder is atherosclerosis.
177. (New) The method of claim 173, further comprising a step of measuring serum LDL-cholesterol, serum VLDL-cholesterol, serum total cholesterol, serum apolipoprotein B, serum triglycerides, or serum Lipoprotein(a).
178. (New) The method of any one of claims 163-177, wherein the antisense oligonucleotide is administered intravenously.
179. The method of any one of claims 163-177, wherein the antisense oligonucleotide is administered subcutaneously.
180. (New) A method of lowering serum cholesterol levels in a human comprising administering to said human a therapeutically effective amount of the antisense oligonucleotide of claim 142.

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181. (New) The method of claim 180 wherein the serum cholesterol levels are serum LDL-cholesterol levels.
182. (New) The method of claim 180, wherein the serum cholesterol levels are serum VLDL-cholesterol levels.
183. (New) The method of claim 180, wherein the serum cholesterol levels are serum total cholesterol levels.
184. (New) A method of lowering lipoprotein levels in a human comprising administering to said human a therapeutically effective amount of the antisense oligonucleotide of claim 142.
185. (New) The method of claim 184, wherein the lipoprotein levels are low density lipoprotein levels.
186. (New) The method of claim 184, wherein the lipoprotein levels are very low density lipoprotein levels.
187. (New) The method of claim 184, wherein the lipoprotein levels are Lipoprotein(a) levels.
188. (New) A method of lowering serum apolipoprotein B levels in a human comprising administering to said human a therapeutically effective amount of the antisense oligonucleotide of claim 142.
189. (New) The method of claim 188, wherein the serum apolipoprotein B is apolipoproteinB-100.
190. (New) A method of treating a human having a cardiovascular disease or disorder comprising administering to said human a therapeutically effective amount of the antisense oligonucleotide of claim 142.
191. (New) The method of claim 190, wherein the disease or disorder is abnormal lipid metabolism, abnormal cholesterol metabolism, or abnormal triglyceride metabolism.
192. (New) The method of claim 190, wherein the disease or disorder is hypercholesterolemia, hyperlipidemia, or hypertriglyceridemia.

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193. (New) The method of claim 190, wherein the disease or disorder is atherosclerosis.
194. (New) The method of claim 190, further comprising a step of measuring serum LDL-cholesterol, serum VLDL-cholesterol, serum total cholesterol, serum apolipoprotein B, serum triglycerides, or serum Lipoprotein(a).
195. (New) The method of any one of claims 180-194, wherein the antisense oligonucleotide is administered intravenously.
196. The method of any one of claims 180-194, wherein the antisense oligonucleotide is administered subcutaneously.